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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,588	01/22/2007	Martin Andrew Crockard	30986/40924	7390

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EXAMINER	
SHAW, AMANDA MARIE	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,588	CROCKARD ET AL.	
	Examiner	Art Unit	
	Amanda Shaw	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *6,7 and 10-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,9,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/22/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-15 are currently pending.

Claims 4, 5, 8, and 9 have been amended.

Claims 14-15 are newly presented.

Applicant's election of Group I (claims 1-5, 8, 9, 14, and 15) in the reply filed on February 16, 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 6-7 and 10-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on February 16, 2010.

Applicants are reminded that for any amendment being filed in response to a restriction or election of species requirement any subsequent amendment, any claims which are non elected must have the status identifier (withdrawn). In the instant case claims 6-7 and 10-13 do not have the status identifier (withdrawn). In order to be responsive to this office action Applicants should amend the claims by indicating that claims 6-7 and 10-13 are withdrawn.

Claim Rejections - 35 USC § 112 1st paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8, 9, 14, and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for determining the presence of or the risk of breast cancer in a human patient comprising the steps of (i) isolating a breast tissue sample from the patient, (ii) assaying said breast tissue sample to detect the level of the gene comprised within the sequence of SEQ ID NO: 1 in said breast tissue sample, and (iii) and determining that said human patient has breast cancer or has a risk of breast cancer when the level of said gene is significantly up regulated in comparison to the level of said gene in normal control breast tissue samples.

does not reasonably provide enablement for a method for the detection of the presence of or the risk of any type of cancer comprising the steps of (i) isolating any type of sample of the patient's genome; and (ii) detecting the presence or expression of the gene comprised within the sequence identified herein as SEQ ID NO: 1, wherein the presence or expression of the gene indicates the presence of or the risk of cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of the Invention

The claims are drawn to a method for the detection of the presence of or the risk of cancer in a patient. The method comprises: (i) isolating a sample of the patient's

genome; and (ii) detecting the presence or expression of the gene comprised within the sequence identified herein as SEQ ID NO: 1, wherein the presence or expression of the gene indicates the presence of or the risk of cancer. The nature of the invention requires a reliable association between the presence or expression of the gene and the presence of or the risk of cancer.

Scope of the Claims:

The claims are broadly drawn to a method for the detection of the presence of or the risk of ANY type of cancer (i.e., breast cancer, lung cancer, medulloblastoma, colon cancer, melanoma etc). Only claims 4, 9, and 15 are limited to a specific type of cancer wherein the cancer is breast cancer.

The claims require a step of isolating a sample of the patient's genome. This broadly encompass isolating ANY type of sample (i.e., breast tissue, lung tissue, brain tissue, hair, blood etc). Only claim 3 is limited to specific types of samples wherein the sample is obtained from breast tissue, the uterus or testis.

The claims broadly state that the presence or the expression of the gene indicates the presence of or the risk of cancer. Thus the claims encompass detecting the presence of the gene or any level of expression of the gene.

Teachings in the Specification and Examples:

Here it is noted that the gene located in SEQ ID NO: 1 has the sequence of SEQ ID NO: 2. This gene is referred to in the specification as DD11.

The specification (page 8) teaches that differential gene expression between matched pairs of normal mammary and tumor tissue from the same donor was carried

out. A number of differentially expressed gene fragments were isolated and one of these fragments, referred to herein as DD11, was significantly up regulated in breast tumor tissue samples from a number of donors. The specification (page 11) teaches that sequence analysis followed by database interrogation determined that DD11 was not homologous to known genes or proteins in the EMBL and SWISSPROT databases, therefore it was regarded as potentially novel. However it was 100% homologous, after removal of the poly-A tail, to a clone (RP11875011) from chromosome 8 of the human genome (Accession Number AC107959).

The specification (page 11) teaches that the DD11 fragment was further screened using cDNA populations derived from a number of matched breast tumor tissues donated by other patients. Of the donor samples screened, 6 out of 9 exhibited notable increases in expression, confirming DD11 to be a putative molecular marker for the presence of breast tumor (FIG. 1). This analysis was substantiated by the molecular signature analysis of all currently available matched breast tissue samples, as follows:

Increased in tumor: 10 out of 19 (52.6%)
Increased in normal: 1 out of 19 (5.3%)
No discernable difference: 7 out of 19 (36.8%)
No expression evident: 1 out of 19 (5.3%)

Accordingly the specification is enabled for A method for determining the presence of or the risk of breast cancer in a human patient comprising the steps of (i) isolating a breast tissue sample from the patient, (ii) assaying said breast tissue sample

to detect the level of the gene comprised within the sequence of SEQ ID NO: 1 in said breast tissue sample, and (iii) and determining that said human patient has breast cancer or has a risk of breast cancer when the level of said gene is significantly up regulated in comparison to the level of said gene in normal control breast tissue samples.

State of the Art and the Unpredictability of the Art:

The level of skill in the art is deemed to be high. However the unpredictability with regard to correlating the presence or expression level of a particular gene with cancer is even higher. The unpredictability is demonstrated by the instant specification and the post filing date art.

For example the claims encompass a method for the detection of the presence of or the risk of ANY type of cancer. The claims state that the presence or expression of the DD11 indicates the presence of or the risk of cancer. However since the specification (page 12) teaches that ovary, colon, stomach, liver, lung, bladder, and pancreas tumors do not even express DD11, clearly the presence of or expression of DD11 can not be used to detect the presence of or the risk of these cancers. As such one of skill in the art would conclude that it is highly unpredictable if the claimed method could be used to detect the presence of or risk of ANY type of cancer.

Regarding breast cancer the specification teaches that DD11 was significantly up regulated in breast tumor tissue samples. While this may be true it is highly unpredictable if the just the presence of DD11 is indicative of the presence of or the risk of breast cancer. Further it is highly unpredictable if any level of expression of DD11 is

indicative of the presence of or the risk of breast cancer. The results presented in the specification (page 11) and in Fig 1 demonstrate that DD11 is expressed in normal breast tissue and tumor breast tissue. The data on DD11 expression is as follows:

Increased in tumor: 10 out of 19 (52.6%)

Increased in normal: 1 out of 19 (5.3%)

No discernable difference: 7 out of 19 (36.8%)

No expression evident: 1 out of 19 (5.3%)

Since DD11 is expressed in normal breast tissue it is highly unpredictable if one of skill in the art could detect the presence of breast cancer or the risk of breast cancer by only detecting the presence of DD11 in a breast tissue or by detecting any level of expression of DD11 in a breast tissue.

Because the claims encompass detecting the expression level of DD11 in ANY type of sample it is relevant to point out the unpredictability in comparing gene expression among different tissues. While the genetic information is the same in all tissues that constitute a multicellular organism, the expression of functions encoded by the genome varies significantly in different tissues. In fact Whitehead (Genome Biology 2005 Vol 6 Issue 2 Article R13) teaches that variation in gene expression is extensive among tissues (abstract). Whitehead further teaches that many different cancers have unique tissue specific patterns of gene expression (page 1, col 2). Here it is noted that with regard to the breast cancer patients the specification does not teach that DD11 was significantly up regulated in other types of tissues samples (i.e. non breast tissue samples) obtained from those patients. Thus in the absence of evidence to the contrary

it is highly unpredictable if it is possible to detect breast cancer by detecting the expression level of DD11 in non breast tissue samples.

Quantity of Experimentation:

In the instant case a large amount of experimentation would be required to make and use the invention as broadly claimed. Such experimentation would require a large case: control study to demonstrate a robust and reliable association between the presence of or expression of DD11 in a representative number of different types of cancer. Such experimentation would be extensive. While methods for analyzing the presence of a gene and gene expression are known in the art, such methods provide only the general guidelines that allow researchers to randomly search for genes that are differentially expressed in certain diseases (such as cancer). The results of performing such methodology are highly unpredictable. The specification has provided only an invitation to experiment.

Conclusions:

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the guidance provided by the applicant and the specific examples, it is the conclusion that an undue amount of experimentation would be required to make and use the invention.

Conclusion

3. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda Shaw whose telephone number is (571)272-8668. The examiner can normally be reached on Mon-Thurs 8:00 TO 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amanda Shaw/
Examiner 1634